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Remarks

Applicant would like to thank the Examiner for the telephonic interview of May 25, 2004, with applicant's attorneys, Robert N. Young and Kathryn E. Cox, in which all of the current rejections in the present case were discussed. During the interview, the Examiner and applicant's attorneys came to a general agreement regarding the basis of the new paragraphs being added to the specification originating in Examples 1-4 of the provisional application. The Examiner and applicant's attorneys also reached a general agreement concerning the substance of claim amendments that may overcome the rejections based on a teaching by Van Ness et al. of the spacer configurations of the present invention.

Claims 22-39 are currently pending in the present application. Claim 22, claim 32, and claim 38 have been amended without prejudice in order to advance to the prosecution of the present application. The amendments to the claims are supported by the application as originally filed, do not add new matter, and are otherwise proper. Support for the amendment to claim 22 can be found throughout the application as originally filed, including without limitation paragraph [0068] through paragraph [0070]. Support for the amendments to claim 32 and claim 38 can also be found throughout the application as originally filed. Specific support for the amendments to claim 32 and claim 38 can be found in newly added paragraph [0074.15]. Applicant respectfully requests entry of these Amendments in their entirety.

These amendments change claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, are presented, with an appropriate defined status identifier. Because the amendments make explicit what was inherent, broaden or do not narrow the scope of the claim 22, claim 32, or claim 38, the claim amendments are not narrowing and the claims are entitled to the same scope either literally or under the Doctrine of Equivalents.

Applicant thanks the Examiner for indicating that the information disclosure statement submitted April 21, 2003 was considered in the present application. Applicant also thanks the Examiner for accepting the amendments to the drawings, the amendments to paragraphs [0052], [0072], [0068], [0069] and [0073], and the amendments of claim 22-32 in regards to the 35 U.S.C. § 112 rejections.

In view of the above amendments and following remarks, applicant respectfully requests reconsideration of the claims and submits that the application is in condition for allowance.

I. Amendment to the Specification

In the Office Action, the Examiner objected to the addition of paragraphs [0074.1] – [0074.18] into the specification as adding new matter. Applicant respectfully traverses. The paragraphs being added come directly from the provisional application on which this utility application is based. Paragraphs [0074.1] – [0074.18] can be found in the description of Examples 1-4 of the provisional patent application. Because the provisional patent application was wholly incorporated by reference in paragraph [0017], applicant respectfully submits that entry of the new paragraphs into the specification of the utility application is proper and requests the Examiner allow the entry.

Regarding the other information incorporated by reference in the patent application, and specifically the material incorporated by reference from Current Protocols in Molecular Biology (Ausubel et al.), all remaining information incorporated by reference is believed to be non-essential at this time. However, applicant reserves the right to amend the present application to include any material incorporated by reference that is considered to be essential.

II. Claim Interpretation

Applicant agrees to the Examiner's interpretation of the meaning of the phrase "wherein the oligonucleotides that are coupled to different bead sets are oligonucleotides with and without a spacer" to mean that "all combinations of oligonucleotides with and without spacers coupled to bead sets are permissible in the claimed invention so long as the claimed methods can be effectively performed.

Applicant disagrees with the Examiner's statement that random bases may include "any bases." Using the Examiner's definition would render the claimed methods inoperable. As used in the invention, the random bases of the spacer may include all bases except those bases that are complementary to the target oligonucleotide 5' or 3' of where the oligonucleotide

hybridizes with the target oligonucleotide. Thus, the random bases of the spacer may include all bases so long as the claimed methods can be effectively performed.

III. Claim Rejections

A. 35 U.S.C. §102(e)

In the Office Action, claims 22-29 and 31-38 were rejected under 35 U.S.C. § 102(e) as being anticipated by Van Ness et al. (U.S. Patent No. 6,361,940). Applicant respectfully traverses. Van Ness et al. cannot anticipate any of the present claims because Van Ness et al. fail to teach or suggest every element of the present claims. Specifically, Van Ness et al. cannot anticipate the present claims because they do not teach the spacer of the presently claimed methods. In amended claim 22, the “complementary regions of the oligonucleotides flank the spacer [and the] complementary regions of the oligonucleotides hybridize with a contiguous sequence on the target oligonucleotide.” Thus, the spacer of the present claims is located internally to an oligonucleotide sequence that is generally complementary to a target oligonucleotide and does not replace any of the bases in the oligonucleotide sequence. As such, the present spacer only lengthens the size of the molecule by separating two portions of a single oligonucleotide probe sequence complementary to a contiguous sequence on the target oligonucleotide. The nucleotide residues on the ends of the complementary sequence flanking the spacer become adjacent to each other when the oligonucleotide hybridizes with a target oligonucleotide.

In contrast, the “specificity spacer” in Van Ness et al. replaces a portion of an oligonucleotide complementary to a target sequence. Van Ness et al. clearly state “the base analog replaces a G, C, or T base in a probe or primer” and “base analogs... maintain essentially the ‘natural’ separation between adjacent nucleotides [and] have a moiety with approximately the same spatial requirements of a G, C, A, or T base.” Column 43, lines 46-47 and lines 34-38, respectively. See also, the sequence listing which states “N is an unnatural nucleotide (i.e., a nucleotide having a chemical moiety which is not one of A,G,C,T or U at the position normally occupied by A,G,C,T or U) or a molecular spacer that provides an equal linear distance, as a natural nucleotide, along the DNA phosphate sugar backbone.” Accordingly, the nucleotide residues that are adjacent to the ends

of the specificity spacer are separated from each other by the length of the specificity spacer when the oligonucleotide hybridizes with a target.

Furthermore, the specificity spacer of Van Ness et al. cannot encompass an additional 20 “bases” in the middle of a complementary oligonucleotide sequence. As acknowledged in the Office Action, Van Ness et al. teach a specificity spacer having a chain of 2-5 carbons. Col. 40, line 54. Because Van Ness et al. demonstrate two of these five carbons bonding together to form a 5-6 membered ring base analog, by definition only two base analogs are capable of forming using five carbons. Col. 41, line 10. Van Ness et al. further teach that the specificity spacers cannot be adjacent to each other. Col. 41, line 42. Therefore, a specificity spacer in Van Ness can only provide two base analogs and cannot be 20 “bases” long.

Accordingly, Van Ness et al. fail to teach or suggest all of the elements of independent claim 22 and applicant respectfully requests the Examiner withdraw this rejection.

Concerning the rejection of claims 23, 24-26, 27, 28, 29, 31, 32, 33-34, 35, 36, and 37-38 as anticipated by Van Ness et al., applicant respectfully traverses. Because Van Ness et al. do not teach or suggest all of the elements of the independent claim, Van Ness et al. cannot teach or suggest all of the elements of the claims that depend from that independent claim. For the foregoing reason, applicant respectfully requests the Examiner withdraw the anticipation rejection to claims 23, 24-26, 27, 28, 29, 31, 32, 33-34, 35, 36, and 37-38.

Furthermore, regarding claims 32 and 38 as amended, Van Ness et al. fail to teach or suggest any assay using beads labeled with fluorescent ratios. Although the Office Action stated that “Van Ness et al. teach oligonucleotides... coupled to different bead sets labeled with fluorescent labels such as BODIPY, TAMRA or Texas Red... (col. 83, lines 10-67),” Van Ness et al. make it clear in the cited example that the probe oligonucleotides, not the solid bead, is fluorescently labeled when they state “[e]ach probe oligonucleotide is labeled with either BODIPY, TAMRA or Texas Red.” Column 83, 29-30 (emphasis added). In fact, the fluorescently labeled probe oligonucleotide is not even immobilized on the solid support because only the “‘target’ oligonucleotide was immobilized on a set of solid supports.” Column 83, lines 19-21 (parenthetical omitted). Accordingly, the fluorescent label stays with the probe oligonucleotide and not the solid support, which Van Ness et al. make clear when they state that the probe oligonucleotide was denatured and the “solution [containing the denatured, labeled probe] is removed from the incubation tubes and

placed in a black microtiter plate. The plates are then read directly...” Column 83, lines 38-45 (parentheticals omitted). Van Ness et al. also cannot anticipate claims 32 or 38 because they further fail to teach or suggest bead sets that have a fluorescence color ratio. Because a ratio is a comparison between two different things, in order to have a fluorescence color *ratio*, the beads of claims 32 or 38 are labeled with at least two different fluorescent labels. Nowhere do Van Ness et al. teach a fluorescently labeled bead, much less a bead with at least two fluorescent labels. Accordingly, Van Ness et al. cannot anticipate dependent claims 32 and 38 because Van Ness et al. both fail to teach or suggest all of the elements of independent claim 22 from which claims 32 and 38 depend and Van Ness et al. fail to teach or suggest beads having a fluorescent ratio. Therefore, even if Van Ness et al. anticipated the independent claim from which claims 32 and 38 depend, which they do not, Van Ness et al. could not anticipate these claims as amended. Thus, applicant respectfully requests the Examiner withdraw the rejection and allow the claims to issue.

Also, regarding claim 33 and claim 34, the Office Action states that Van Ness et al. teach the spacer as being a nucleic acid base. However, Van Ness never discloses the use of a nucleic acid base as the spacer. As shown in the dictionary definition, a nucleic acid is “any of various acids (as DNA or RNA) that are composed of nucleotide chains.” (Merriam Webster’s Collegiate Dictionary, 10th ed. 1997). A nucleotide can be defined as “any of several compounds that consist of a ribose or deoxyribose sugar joined to a purine or pyrimidine base and to a phosphate group and that are the basic structural units of nucleic acids (as RNA and DNA).” *Id.* Van Ness et al. do not teach or suggest the use of a nucleic acid base as the spacer, but instead teach the use of a spacer containing an abasic residue or a base analog (or both). A base analog may take up the same amount of space as a nucleic acid base but it is NOT a nucleic acid as defined by those having skill in the art. An analog is defined as “a chemical compound that is structurally similar to another but differs slightly in composition (as in the replacement of one atom by an atom of a different element or in the presence of a particular functional group).” *Id.* Thus, Van Ness et al. disclose the use of something similar but not the same as a nucleic acid base for use in the specificity spacer. Because Van Ness et al. do not teach a nucleic acid base for use in the spacer, they cannot anticipate claim 33 and claim 34 of the present invention. Therefore, applicant respectfully requests the rejection to claim 33 and claim 34 be withdrawn and the claims allowed to issue.

B. 35 U.S.C § 103

a. Claims 22-29 and 31-38

In the Office Action claims 22-29 and 31-38 were rejected as obvious over Kaneoka et al. and Van Ness et al. Applicant respectfully traverses. In order to “establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art.” MPEP §2143.03. Applicant agrees with the Examiner’s statement in the Office Action that it is a combination of references, not references taken individually, that render the claims obvious. However, as stated in § 2143 of the MPEP, “[t]he prior art reference (or references when combined) must teach or suggest all of the claim limitations.” (emphasis added). Based on this standard, the combination of Kaneoka et al. and Van Ness et al. cannot render the rejected claims prima facie obvious because this combination of references fails to teach or suggest the present spacer configuration, an element of all of the rejected claims. As stated above, Van Ness et al. do not teach or disclose the present spacer configuration. Nor do Kaneoka et al. overcome this deficiency as even the Examiner admits that “Kaneoka et al. do not teach oligonucleotides with and without spacers coupled to different bead sets.” Accordingly, the combination Kaneoka et al. and Van Ness et al. cannot state a proper prima facie case of obviousness and applicant respectfully requests the Examiner withdraw this rejection.

b. Claim 30

Claim 30 was rejected as obvious over Kaneoka et al. and Van Ness et al. further in view of Nolan et al. However, Nolan et al. cannot overcome the deficiencies of Kaneoka et al. or Van Ness et al. because they also fail to teach or suggest the claimed spacer arrangement. Accordingly applicant respectfully requests the Examiner withdraw this rejection and allow the claim to issue.

c. Claims 22-29 and 31-39

Claims 22-29 and 31-39 were rejected in the Office Action as obvious over Armstrong et al. and Van Ness et al. Applicant respectfully traverses this rejection. As discussed above, Van Ness et al. do not teach all of the elements of the present claims because Van Ness et al. do not teach the present spacer configuration. Armstrong et al. cannot overcome this

deficiency because, as admitted by the Examiner, Armstrong et al. "do not teach oligonucleotides with and without spacers." Furthermore, with respect to claims 32 and 38, Van Ness et al. do not teach bead sets having a fluorescent color ratio. Accordingly, this combination of references cannot render the rejected claims prima facie obvious. In light of this, applicant respectfully requests the Examiner withdraw the obviousness rejection to claims 22-29 and 31-39.

d. Claim 31

Claim 31 was rejected in the Office Action as obvious over Armstrong et al. and Van Ness et al. further in view of Long. Applicant respectfully traverses the rejection of claim 31. Neither Armstrong et al. nor Van Ness et al. teach or suggest the spacer configuration of claim 22 from which claim 31 depends. Therefore, Armstrong et al. and Van Ness et al. cannot teach each and every element of the rejected claim. Long does not overcome this deficiency because it also fails to teach or suggest a spacer as presently claimed. Accordingly, applicant respectfully requests the Examiner withdraw this rejection and allow claim 31 to issue.

CONCLUSION

In view of the above remarks, it is respectfully submitted that this application is in condition for allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to telephone the undersigned at the number listed below if the Examiner believes such would be helpful in advancing the application to issue.

Respectfully submitted,

Date July 19, 2004

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late, fr. Gk *ana-* + *chronos* time] (ca. 1646) 1: an error in chronology; esp: a chronological misplacing of persons, events, objects, or customs in regard to each other 2: a person or a thing that is chronologically out of place; esp: one from a former age that is incongruous in the present — **anach-ro-nis-tic** \ə-nə-krə-nis-tik/ also **ana-chron-ic** \ə-nə-krə-nik/ *adj* — **anach-ro-nis-tic-al-ly** \ə-nə-krə-nis-tik(-ə-lē) *adv* — **anach-ro-nous** \ə-nə-krə-nəs/ *adj* — **anach-ro-nous-ly** *adv*

ana-clit-ic \ə-nə-kli-tik/ *adj* [Gk *anaklitos*, verbal of *anaklinein* to lean upon, fr. *ana-* + *klinein* to lean — more at **LEAN**] (1922) 1: of, relating to, or characterized by the direction of love toward an object (as the mother) that satisfies nonsexual needs (as hunger)

ana-co-lu-thon \ə-nə-kə-lü-thən/ *n*, *pl* -thə \-thə/ also -thons [LL, fr. LGk *anakolouthon* inconsistency in logic, fr. Gk, neut. of *anakolouthos* inconsistent, fr. *an-* + *akolouthos* following, fr. *ha-*, *a-* together + *keleuthos* path] (ca. 1706): syntactical inconsistency or incoherence within a sentence; esp: a shift in an unfinished sentence from one syntactic construction to another (as in "you really ought—well, do it your own way") — **ana-co-lu-thic** \-thik/ *adj* — **ana-co-lu-thi-cal-ly** \-thi-k(-ə-lē) *adv*

ana-con-da \ə-nə-kän-də/ *n* [prob. modif. of Sinhalese *henakandayā*, a slender green snake] (1768): a large semiaquatic constricting snake (*Eunectes murinus*) of the boa family of tropical So. America that may reach a length of 30 feet (9.1 meters); broadly: any of the large constricting snakes

anae-re-on-tic \ə-nə-krē-ān-tik/ *n* (1656): a poem in the manner of Anacreon; esp: a drinking song or light lyric

Anacreontic *adj* [L *Anacreonticus*, fr. *Anacreont-*, *Anacreon* Anacreon, fr. Gk *Anakreont-*, *Anakreōn*] (1611) 1: of, relating to, or resembling the poetry of Anacreon 2: convivial or amatory in tone or theme

ana-cru-sis \ə-nə-krü-səs/ *n*, *pl* -cru-ses \-sēz/ [NL, fr. Gk *anakrousis* beginning of a song, fr. *anakrouein* to begin a song, fr. *ana-* + *krouein* to strike, beat; akin to Lith *krausyti* to strike] (1830) 1: one or more syllables at the beginning of a line of poetry that are regarded as preliminary to and not a part of the metrical pattern 2: UPBEAT; *specif*: one or more notes or tones preceding the first downbeat of a musical phrase

ana-dama bread \ə-nə-da-mə/ *n* [origin unknown] (1954): a leavened bread made with flour, cornmeal, and molasses

ana-dem \ə-nə-dem/ *n* [L *Anadema*, fr. Gk *anadēma*, fr. *anadein* to wreath, fr. *ana-* + *dein* to bind — more at **DIADDEM**] (1604) *archaic*: a wreath for the head: **GARLAND**

ana-di-plo-sis \ə-nə-də-plō-səs, ə-nə-(dī)-plō/ *n*, *pl* -plo-ses \-sēz/ [LL, fr. Gk *anadiplosis*, lit., repetition, fr. *anadiploō* to double, fr. *ana-* + *diploō* to double — more at **DIPLOMA**] (ca. 1550): repetition of a prominent and usu. the last word in one phrase or clause at the beginning of the next (as in "rely on his honor—honor such as his?")

anad-ro-mous \ə-nə-drə-məs/ *adj* [Gk *anadromos* running upward, fr. *anadromēin* to run upward, fr. *ana-* + *dromēin* to run — more at **DROMEDARY**] (ca. 1753): ascending rivers from the sea for breeding (shad are ~) — compare **CATADROMOUS**

anae-mia, **anae-mic** chiefly *Brit var* of **ANEMIA**, **ANEMIC**

anae-ro-be \ə-nə-rōb; (Jan-a)-rōb, -ē(-ə)-rō/ *n* [ISV] (1884): an anaerobic organism

anae-ro-bic \ə-nə-rō-bik; an-a(-ə)-, -ē(-ə)-/ *adj* (ca. 1881) 1: living, active, occurring, or existing in the absence of free oxygen (~ respiration) 2: of, relating to, or being activity in which the body incurs an oxygen debt (~ exercise) 2: relating to or induced by anaerobes — **anae-ro-bi-cal-ly** \-bi-k(-ə-lē) *adv*

anae-ro-bi-osis \ə-nə-rō(-bi)-ō-sis, -bē; an-a(-ə)-, -ē(-ə)-/ *n*, *pl* -oses \-ō-sēz/ [NL] (ca. 1889): life in the absence of air or free oxygen

anae-the-sia, **anae-thet-ic** chiefly *Brit var* of **ANESTHESIA**, **ANESTHETIC**

ana-gen-e-sis \ə-nə-jē-ne-sis/ *n* [NL] (1889): evolutionary change producing a single lineage in which one taxon replaces another without branching — compare **CLADOGENESIS**

ana-glyph \ə-nə-glif/ *n* [LL *anaglyphus* embossed, fr. Gk *anaglyphos*, fr. *anaglyphein* to emboss, fr. *ana-* + *glyphein* to carve — more at **CLEAVE**] (1651) 1: a sculptured, chased, or embossed ornament worked in low relief 2: a stereoscopic motion or still picture in which the right component of a composite image usu. red in color is superimposed on the left component in a contrasting color to produce a three-dimensional effect when viewed through correspondingly colored filters in the form of spectacles — **ana-glyph-ic** \ə-nə-gli-fik/ *adj*

ana-gno-ris-is \ə-nə-gnō-ris-is, -rī; an-a(-ə)-, -ē(-ə)-/ *n*, *pl* -ris-es \-rīs-sēz/ [NL] (ca. 1889): life in the absence of air or free oxygen

ana-gno-ris-is \ə-nə-gnō-ris-is, -rī; an-a(-ə)-, -ē(-ə)-/ *n*, *pl* -ris-es \-rīs-sēz/ [NL] (ca. 1889): life in the absence of air or free oxygen

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ana-gno-ris-is \ə-nə-gnō-ris-is, -rī; an-a(-ə)-, -ē(-ə)-/ *n*, *pl* -ris-es \-rīs-sēz/ [NL] (ca. 1889): life in the absence of air or free oxygen



anaconda

anagram *vi* -grammed; -gram-ming (1630) 1: ANAGRAMMATIZE 2: to rearrange (the letters of a text) in order to discover a hidden message

an-a-gram-ma-tize \ə-nə-grə-mə-tīz/ *vi* -tized; -tiz-ing (1588): to transpose (as letters in a word) so as to form an anagram — **an-a-gram-ma-ti-za-tion** \-grə-mə-tə-zā-shən/ *n*

anal \ə-nəl/ *adj* (1769) 1: of, relating to, or situated near the anus (~ fin) 2: a: of, relating to, characterized by, or being the stage of psychosexual development in psychoanalytic theory during which the child is concerned esp. with its feces b: of, relating to; characterized by, or being personality traits (as parsimony, meticulousness, and ill humor) considered typical of fixation at the anal stage of development (~ disposition) (~ neatness) — **anal-ly** \-nəl-ē/ *adv*

anal-cime \ə-nal-sēm/ *n* [F, fr. Gk *analkimos* weak, fr. *an-* + *alkimos* strong, fr. *alkē* strength] (1803): a white or slightly colored mineral that consists of hydrated silicate of sodium and aluminum and occurs in various igneous rocks in massive form or in crystals

anal-cite \ə-nal-sīt/ *n* (1868): **ANALCIME**

ana-lecta \ə-nəl-ek(-tə) also **ana-lect-ta** \ə-nəl-ek(-tə) *n*, *pl* [NL *analekta*, fr. Gk *analekta*, neut. pl. of *analektos*, verbal of *analegein* to collect, fr. *ana-* + *legein* to gather — more at **LEGEND**] (1652): selected miscellaneous written passages

ana-lem-ma \ə-nə-le-mə/ *n* [L *sundial* on a pedestal, fr. Gk *analemma*, lofty structure, sundial, fr. *analembanein* to take up, restore, fr. *ana-* + *lambanein* to take — more at **LATCH**] (1832): a plot or graph of the position of the sun in the sky at a certain time of day (as noon) at one locale measured at regular intervals throughout the year that has the shape of a figure 8; also: a scale (as on a globe or sundial) based on such a plot that shows the sun's position for each day of the year or that allows local mean time to be determined — **ana-lem-mat-ic** \ə-nə-le-mə-tik, -lə/ *adj*

ana-lep-tic \ə-nə-lep-tik/ *n* [Gk *analeptikos*, fr. *analembanein*] (1671): a drug that stimulates the central nervous system — **analeptic** *adj*

an-al-ge-sia \ə-nəl-jē-zh(-ē)-, -zē-ə/ *n* [NL, fr. Gk *analgēsia*, fr. *an-* + *algēsis* sense of pain, fr. *algēin* to suffer pain, fr. *algos* pain] (ca. 1706): insensibility to pain without loss of consciousness — **an-al-ge-sic** \-jē-zik, -sik/ *adj* or *n* — **an-al-ge-tic** \-jē-tik/ *adj* or *n*

anal-ly \ə-nə-lē/ *n*, *pl* -ties (1939): the psychological state or quality of being anal

ana-log \ə-nəl-ŏg, -äg/ *adj* (1948) 1: of, relating to, or being an analogue 2: a: of, relating to, or being a mechanism in which data is represented by continuously variable physical quantities b: of or relating to an analog computer c: being a timepiece having hour and minute hands

analog computer *n* (1948): a computer that operates with numbers represented by directly measurable quantities (as voltages or rotations) — compare **DIGITAL COMPUTER**, **HYBRID COMPUTER**

ana-log-i-cal \ə-nəl-ŏ-jī-kəl/ also **ana-log-ic** \-jīk/ *adj* (1609) 1: of, relating to, or based on analogy 2: expressing or implying analogy — **ana-log-i-cal-ly** \-jī-k(-ə-lē) *adv*

ana-log-ist \ə-nə-lŏ-jist/ *n* (ca. 1828): one who searches for or reasons from analogies

anal-o-gize \-jīz/ *vb* -gized; -giz-ing *vi* (1655): to use or exhibit analogy ~ *vi*: to compare by analogy

anal-o-gous \ə-nə-lŏ-gəs/ *adj* [L *analogus*, fr. Gk *analogos*, lit., proportionate, fr. *ana-* + *logos* reason, ratio, fr. *legein* to gather, speak — more at **LEGEND**] (1646) 1: showing an analogy or a likeness that permits one to draw an analogy 2: being or related to as an analogue *syn* see **SIMILAR** — **anal-o-gous-ly** *adv* — **anal-o-gous-ness** *n*

ana-logue or **ana-log** \ə-nəl-ŏg, -äg/ *n* [F *analogue*, fr. *analogue* analogous, fr. Gk *analogos*] (1826) 1: something that is analogous or similar to something else 2: an organ similar in function to an organ of another animal or plant but different in structure and origin 3: *usu* **analog**: a chemical compound that is structurally similar to another, but differs slightly in composition (as in the replacement of one atom by an atom of a different element or in the presence of a particular functional group) 4: a food product made by combining a less expensive food (as soybeans or whitefish) with additives to give the appearance and taste of a more expensive food (as beef or crab)

ana-logue chiefly *Brit var* of **ANALOG**

anal-o-gy \ə-nə-lŏ-jē/ *n*, *pl* -gies (15c) 1: inference that if two or more things agree with one another in some respects they will prob. agree in others 2: a: resemblance in some particulars between things otherwise unlike b: comparison based on such resemblance 3: correspondence between the members of pairs or sets of linguistic forms that serves as a basis for the creation of another form 4: correspondence in function between anatomical parts of different structure and origin — compare **HOMOLOGY** *syn* see **LIKENESS**

an-al-ph-a-bet \ə-nəl-fə-bet, -bət/ *n* [Gk *analphabētos* not knowing the alphabet, fr. *an-* + *alphabētos* alphabet] (ca. 1889): one who cannot read: **ILLITERATE** — **an-al-ph-a-bet-ic** \ə-nəl-fə-bet-ik/ *adj* or *n* — **an-al-ph-a-bet-ism** \ə-nəl-fə-bet-iz-əm/ *n*

anal-y-sand \ə-nə-lŏ-sənd/ *n* [analysis + and (as in *multiplacand*)] (1917): one who is undergoing psychoanalysis

ana-ly-se chiefly *Brit var* of **ANALYZE**

ana-ly-sis \ə-nə-lŏ-sis/ *n*, *pl* -yses \-sēz/ [NL, fr. Gk, fr. *analein* to break up, fr. *ana-* + *lyein* to loosen — more at **LOSE**] (1581) 1: separation of a whole into its component parts 2: a: the identification or separation of ingredients of a substance b: a statement of the constituents of a mixture 3: a: proof of a mathematical proposition by assuming the result and deducing a valid statement by a series of reversible steps b: (1): a branch of mathematics concerned mainly with functions and limits (2): **CALCULUS** 1b 4: a: an examination of a complex, its elements, and their relations b: a statement of such an analysis 5: a: a method in philosophy of resolving complex expressions into simpler or more basic ones b: clarification of an expression by an elucidation of its use in discourse 6: the use of function words

\ə/ abut \ʌ/ kitten, F table \ər/ further \ə/ ash \ā/ ace \ā/ mop, mar \ā/ out \ch/ chin \et/ bet \ē/ easy \g/ go \i/ hit \i/ ice \j/ job \j/ sing \ŏ/ go \ŏ/ law \ŏi/ boy \th/ thin \th/ the \ü/ foot \ü/ foot \y/ yet \zh/ vision \ā, ē, °, œ, ue, ū, see Guide to Pronunciation

tant point or indicate a transition (as of ideas) 4: SOMETIMES (~ one and ~ another) 5: under the present circumstances 6: at the time referred to (~ the trouble began)

now conj (bef. 12c): in view of the fact that: SINCE — often followed by *that* (~ that we are here)

now n (12c): the present time or moment (been ill up to ~)

now adj (14c): 1: of or relating to the present time: EXISTING (the ~ president) 2: a: excitingly new (~ clothes) b: constantly aware of what is new (~ people) (the ~ generation)

NOW account \ˈnau-ə-ˌnɔː\ *n* [negotiable order of withdrawal] (1974): a savings account on which checks may be drawn

now-a-days \ˈnau-(ə)-ˌdæz\ *adv* [ME *now a dayes*, fr. *now + a dayes* during the day] (14c): at the present time

now and then adv (15c): from time to time: OCCASIONALLY (*now and then* we go off to the country)

no-way adv (13c): 1 \ˈnɔː-wə\ or *no-ways* \-wəz\ : NOWISE 2 *usu no way* \-wə\ : NO — used emphatically

no-where \ˈnɔː-hwɛr-, -hwɛr-, -hwɔr or without h\ *adv* (bef. 12c): 1: not in or at any place 2: to no place

nowhere n (1831): 1: a nonexistent place 2: an unknown, distant, or obscure place or state (rose to fame out of ~) — *miles from nowhere*: in an extremely remote place

nowhere near adv (15c): not nearly

no-where \ˈnɔː-hwɛr-, -hwɛr-, -hwɔr or without h\ *adv* (ca. 1866) chiefly dial: NOWHERE

no-whither \ˈnɔː-hwi-ˌθɔr-, -wi-ˌθɔr; nɔː-ˌ\ *adv* (bef. 12c): to or toward no place

no-win \ˈnɔː-wɪn-, -wɪn\ *adj* (1962): not likely to give victory, success, or satisfaction: that cannot be won (a ~ situation) (a ~ war)

no-wise \ˈnɔː-wɪz\ *adv* (14c): not at all

now-ness \ˈnau-nəs\ *n* (1674): the quality or state of existing or occurring or of belonging to the present time

nowt \ˈnaut also ˈnɔt\ *dial Eng var of* NOUGHT

nox-i-ous \ˈnɔk-shəs\ *adj* [ME *noxius*, fr. L. *nox* harm; akin to L. *nocere* to harm, *ne-*, *ne-* violent death, Gk *nekros* dead body] (15c): 1 a: physically harmful or destructive to living beings (~ wastes that poison our streams) b: constituting a harmful influence on mind or behavior: morally corrupting (~ doctrines) 2: DISTASTEFUL OBNOXIOUS *syn* see PERNICIOUS — *nox-i-ous-ly adv* — *nox-i-ous-ness n*

noz-zle \ˈnɔz-zəl\ *n* [dim. of *noze*] (1683): 1 a: a projecting vent of something b: a short tube with a taper or constriction used (as on a hose) to speed up or direct a flow of fluid, c: a part in a rocket engine that accelerates the exhaust gases from the combustion chamber to a high velocity 2 *slang*: NOSE

NSAID \ˈen-sed also -səd\ *n* [nonsteroidal anti-inflammatory drug] (1985): a nonsteroidal anti-inflammatory drug (as ibuprofen)

-n't vb comb form: not (isn't)

nth \ˈen(t)h\ *adj* [*n* (indefinite number) + *-th*] (1852): 1: numbered with an unspecified or indefinitely large ordinal number (for the ~ time) 2: EXTREME, UTMOST (to the ~ degree)

n-type \ˈen-ˌtɪp\ *adj* [negative + *type*] (1946): relating to or being a semiconductor in which charge is carried by electrons — compare P-TYPE

nu \ˈnuː, ˈnyuː\ *n* [Gk *ny*, of Sem origin; akin to Heb *nūn* nun] (ca. 1823): the 13th letter of the Greek alphabet — see ALPHABET table

nu-ance \ˈnuː-ˌæns\ *n* [Fr. *nuance*, fr. *nue* cloud, fr. L. *nubes*, perh. akin to W *nudd* mist] (1781): 1: a subtle distinction or variation 2: a subtle quality: NICETY 3: sensibility to, awareness of, or ability to express delicate shadings (as of meaning, feeling, or value) — *nu-anced* \-ˌænt(t)st-, -ˌænt(t)st\ *adj*

nub \ˈnʌb\ *n* [alter. of E dial. *knub*, prob. fr. LG *knubbe*] (1727): 1: KNOB, LUMP 2: NUBBIN 3: GIST, POINT

nub-bin \ˈnʌ-bən\ *n* [perh. dim. of *nub*] (1692): 1: something (as an ear of Indian corn) that is small for its kind, stunted, undeveloped, or imperfect 2: a small *usu* projecting part or bit 3: NUB 3

nub-ble \ˈnʌ-bəl\ *n* [dim. of *nub*] (1818): a small knob or lump — *nub-bly* \-b(ə)-lē\ *adj*

nub-by \ˈnʌ-bi\ *adj* *nub-by-er*, -est [*nub* + *-y*] (ca. 1876): 1: having or being like nubbles 2: having nubs (a ~ knit fabric)

Nu-bi-an \ˈnuː-bi-ən, ˈnyuː-ˌ\ *n* (15c): 1 a: a native or inhabitant of Nubia b: a member of one of the group of dark-skinned peoples that formed a powerful empire between Egypt and Ethiopia from the 6th to the 14th centuries 2: any of several languages spoken in central and northern Sudan — *Nubian adj*

nu-bile \ˈnuː-bil, ˈnyuː-, -bəl\ *adj* [F. fr. L. *nubilis*, fr. *nubere* to marry — more at NUPTIAL] (ca. 1642): 1: of marriageable condition or age 2: sexually attractive — used of a young woman — *nu-bil-i-ty* \ˈnyuː-bi-lə-ti, ˈnyuː-ˌ\ *n*

nu-cel-lus \ˈnuː-se-ləs, ˈnyuː-ˌ\ *n*, *pl* *nu-cel-li* \-ˌse-lɪ\ [NL, fr. L. *nucella* small nut, fr. *nuc*, *nux* nut — more at NUT] (1882): the central and chief part of a plant ovule that encloses the female gametophyte — *nu-cel-lar* \-ˌse-lər\ *adj*

nu-chal \ˈnuː-kəl, ˈnyuː-ˌ\ *adj* [ML *nucha* nape, fr. Ar *nukha* spinal marrow] (1835): of, relating to, or lying in the region of the nape

nucle- or **nucleo-** *comb form* [F *nucle*, *nucleo*, fr. NL *nucleus*] 1: nucleus (nucleoplasm) 2: nucleic acid (nucleoprotein)

nu-cle-ar \ˈnuː-kle-ər, ˈnyuː-, -ˌ\ *adj* (1846): 1: of, relating to, or constituting a nucleus 2 a: of or relating to the atomic nucleus (~ reaction) (~ fuel) (~ waste) (~ energy) c (1): being a reaction (as fission) (2): of, produced by, or involving nuclear weapons (the ~ reaction) (3): armed with nuclear weapons (~ powers) d: of, relating to, or powered by nuclear energy (a ~ submarine) (the ~ debate) (a ~ plant)

usage Though disapproved of by many, pronunciations ending in \-kya-lər\ have been found in widespread use among educated speakers including scientists, lawyers, professors, congressmen, U.S. cabinet members, and at least one U.S. president and one vice president. While most common in the U.S., these pronunciations have also been heard from British and Canadian speakers.

nuclear family n (1947): a family group that consists only of father, mother, and children

nuclear magnetic resonance n (1942): the magnetic resonance of atomic nucleus

nuclear medicine n (1952): a branch of medicine dealing with the use of radioactive materials in the diagnosis and treatment of disease

nuclear membrane n (1888): a double membrane enclosing the nucleus and having its outer part continuous with the endoplasmic reticulum — see CELL illustration

nuclear-powered adj (1948): powered by nuclear energy

nuclear resonance n (1940): the resonance absorption of a ray by a nucleus identical to the nucleus that emitted the gamma ray

nuclear sap n (1877): the clear homogeneous ground substance of a cell nucleus — called also *karyolymph*

nuclear winter n (1983): the chilling of climate that is hypothesized to be a consequence of nuclear war and to result from the global blockage of sunlight by high-altitude dust clouds produced by nuclear explosions

nu-cle-ase \ˈnuː-kle-əs, ˈnyuː-, -ˌ\ *n* (1902): any of various enzymes that promote hydrolysis of nucleic acids

nu-cle-ate \ˈnuː-kle-ət, ˈnyuː-ˌ\ *vb* -at-ed, -at-ing [LL *nucleatus*, fr. *nucleus* to become stony, fr. L. *nucleus* vi (ca. 1864): 1: to form a nucleus: CLUSTER 2: to act as a nucleus for 3: to supply nuclei ~ *vi* 1: to form a nucleus 2: to act as a nucleus 3: to form ~ *nu-cle-ation* \ˈnuː-kle-ə-tən, ˈnyuː-ˌ\ *n* — *nu-cle-ate* \ˈnuː-kle-ət, ˈnyuː-ˌ\ *adj*

nu-cle-ated \ˈnuː-kle-əd, ˈnyuː-ˌ\ or *nu-cle-ate* \ˈnuː-kle-ət, ˈnyuː-ˌ\ *adj* (1845): 1: having a nucleus or nuclei (a ~ cell) 2 *usu nucleate*: originating or occurring at nuclei (a ~ cell) (boiling)

nu-cle-ic acid \ˈnuː-kle-ik-, -ˌklə-, ˈnyuː-ˌ\ *n* [fr. their occurrence in nucleic acids] (1892): any of various acids (as DNA or RNA) that are composed of nucleotide chains

nu-cle-in \ˈnuː-kle-ən, ˈnyuː-ˌ\ *n* (1878): 1: NUCLEOPROTEIN 2: NUCLEIC ACID

nu-cle-o-cap-sid \ˈnuː-kle-ə-ˌkəp-səd, ˈnyuː-ˌ\ *n* (1963): the nucleocapsid and surrounding protein coat in a virus

nu-cle-oid \ˈnuː-kle-ɔɪd, ˈnyuː-ˌ\ *n* (1938): the DNA-containing body of a prokaryotic cell (as a bacterium)

nu-cle-o-lus \ˈnuː-kle-ə-ləs, ˈnyuː-ˌ\ *n*, *pl* -li \-li\ [NL, fr. L. *dim. of nucleus*] (1845): a spherical body of the nucleus of most eukaryotic cells becomes enlarged during protein synthesis, is associated with a nuclear organizer, and contains the DNA templates for ribosomal RNA — see CELL illustration — *nu-cle-o-lar* \-lər\ *adj*

nucleolus organizer n (1939): the specific part of a chromosome with which a nucleolus is associated esp. during its reorganization

nuclear division — called also *nucleolar organizer*: 1: a nuclear partition

nu-cle-on \ˈnuː-kle-ən, ˈnyuː-ˌ\ *n* [ISV] (1923): 1: a nuclear particle: PROTON b: NEUTRON 2: a hypothetical single entity with one unit of isospin that can manifest itself as either a proton or a neutron — *nu-cle-on-ic* \ˈnuː-kle-ə-nɪk, ˈnyuː-ˌ\ *adj*

nu-cle-on-ics \ˈnuː-kle-ə-nɪks, ˈnyuː-ˌ\ *n* *pl* but *sing* or *pl* in constr. (1938): a branch of physical science that deals with nucleons or with all the phenomena of the atomic nucleus

nu-cle-o-phil \ˈnuː-kle-ə-ˌfɪl, ˈnyuː-ˌ\ *n* (1943): a nucleophilic substance (as an electron-donating reagent)

nu-cle-o-philic \ˈnuː-kle-ə-ˌfɪ-lɪk, ˈnyuː-ˌ\ *adj* (1933): 1 of an atom, molecule, or group: having an affinity for atomic nuclei: being an electron donor 2: involving a nucleophilic species (a ~ reaction) — compare ELECTROPHILIC — *nu-cle-o-phil-i-cal-ly* \-lɪ-k(ə)-lē\ *adv* — *nu-cle-o-phil-i-ty* \ˈnuː-kle-ə-ˌfɪ-lɪ-ti\ *n*

nu-cle-o-plasm \ˈnuː-kle-ə-ˌplə-zəm, ˈnyuː-ˌ\ *n* [ISV] (1888): the plasma of a nucleus; esp.: NUCLEAR SAP — *nu-cle-o-plas-mic* \-ˌmɪk\ *adj*

nu-cle-o-protein \ˈnuː-kle-ə-ˌprō-tēn, ˈnyuː-ˌ\ *n* [ISV, irreg. fr. *nucleus*] (1907): a compound that consists of a protein (as a histone) conjugated with a nucleic acid (as a DNA) and that is the principal component of the hereditary material in chromosomes

nu-cle-o-side \ˈnuː-kle-ə-ˌsɪd, ˈnyuː-ˌ\ *n* [ISV *nucle-* + *-ose* + *-side*] (1911): a compound (as guanosine or adenosine) that consists of a purine or pyrimidine base combined with deoxyribose or ribose — found esp. in DNA or RNA

nu-cle-o-some \ˈnuː-kle-ə-ˌsəm, ˈnyuː-ˌ\ *n* (1962): any of the repeating globular units of chromatin that consist of a complex of DNA and histone

nu-cle-o-somal \ˈnuː-kle-ə-ˌsɔ-məl, ˈnyuː-ˌ\ *adj*

nu-cle-o-syn-the-sis \ˈnuː-kle-ə-ˌsɪn(t)-thə-səs, ˈnyuː-ˌ\ *n* [NL] (1908): the production of a chemical element from simpler nuclei (as of drogen) esp. in a star — *nu-cle-o-syn-thet-ic* \-sɪn(t)-thet-ɪk\ *adj*

nu-cle-o-tid-ase \ˈnuː-kle-ə-ˌtɪ-dās, ˈnyuː-ˌ\ *n* (1911): a phosphatase that promotes hydrolysis of a nucleotide (as into a nucleoside and phosphoric acid)

nu-cle-o-tide \ˈnuː-kle-ə-ˌtɪd, ˈnyuː-ˌ\ *n* [ISV, irreg. fr. *nucle-* + *-ide*] (1908): any of several compounds that consist of a ribose or deoxyribose sugar joined to a purine or pyrimidine base and to a phosphate group and that are the basic structural units of nucleic acids (as DNA) — compare NUCLEOSIDE

nu-cle-us \ˈnuː-kle-əs, ˈnyuː-ˌ\ *n*, *pl* *nu-clei* \-ˌkleɪ\ also *nu-cle-i* [NL, fr. L. *nucleus*, dim. of *nux*, *nux* nut — more at NUT] (1700): the small brighter and denser portion of a galaxy or of the head of a comet 2: a central point, group, or mass about which gathering, concentration, or accretion takes place: as a: a cellular organelle (as a nucleus) that is essential to cell functions (as reproduction and protein synthesis) is composed of nuclear sap and a nucleoprotein network from which chromosomes and nucleoli arise, and is enclosed in a definite membrane — see CELL illustration b: a mass of matter or group of nerve cells in the central nervous system characteristic and stable complex of atoms or groups in a molecule: RING (the naphthalene ~) d: the positively charged central part of an atom that comprises nearly all of the atomic mass and consists of protons and neutrons except in hydrogen which consists of a single proton only 3: the peak of sonority in the utterance of a syllable — *nu-clid* \ˈnuː-kli-d, ˈnyuː-ˌ\ *n* [ISV] (1947): a species of atom characterized by the number of its nucleus and hence by the number of protons, the number of neutrons, and the energy content — *nu-clid-ic* \ˈnuː-kli-dɪk, ˈnyuː-ˌ\ *adj*

nude \ˈnuːd, ˈnyuːd\ *adj* *nud-er*; *nud-est* [L *nudus* naked]